

## LETTERS TO THE EDITOR

### Carbamazepine in Reiter's syndrome

EDITOR,—A psoriatic spectrum with Reiter's syndrome as the most severe manifestation occurs with greater frequency in HIV infected individuals.<sup>1</sup> Immunosuppressive therapies for RS are associated with a poor response and increased morbidity.<sup>2</sup> We describe a case where carbamazepine showed an excellent response in an HIV infected patient with Reiter's syndrome.

A 30 year old married man presented with erythematous papules and plaques of 2 months' duration covered with hard limpet-like scales on face, body, and both extremities (fig 1). Palms and soles showed keratoderma blennorrhagicum and subungual hyperkeratosis with distal onycholysis. Both knees and wrists had painful swelling with restriction of movements. With this clinical presentation Reiter's syndrome was inferred. All routine investigations were normal except a raised erythrocyte sedimentation rate of 100 mm in the first hour. x Rays of the affected joints were normal. ELISA for HIV-1 and HIV-2 was positive with two kits (Immunocomb, Tri-dot) and confirmed with western blotting technique (Speciality Rimbax Limited). The absolute helper T lymphocyte count was 435 cells  $\times 10^6/l$ . Human leucocyte antigen B27 and rheumatoid factor were negative. The patient was commenced on prednisolone by mouth 60 mg daily and indomethacin by mouth 25 mg three times daily without any concomitant antiretroviral therapy. New erythematous papules and plaques appeared with no relief in joint pain and swelling.

In seeking an effective treatment, we serendipitously came across the efficacy of carbamazepine in an HIV infected patient with psoriatic erythroderma.<sup>3</sup> We started carbamazepine 200 mg daily in two divided doses in addition to above. The erythema cleared rapidly within 7 days. To confirm the effect of carbamazepine, it was stopped. New lesions similar to the old ones appeared within 3-4 days. Carbamazepine was then reintroduced in the same dose. Erythema cleared again within 7 days followed by scaling and joint swelling and pain. New lesions stopped appearing. Prednisolone was then tapered off rapidly and analgesics were stopped. Carbamazepine was continued in the same dose for 6 months. On follow up at 1 year, the patient showed no recurrence of

skin lesions and synovitis, no change in liver and renal function tests, with no further deterioration in his overall health and no opportunistic infections.

It has been proposed that in genetically predisposed people, the release of neuropeptides like substance P, calcitonin gene related peptide, vasoactive intestinal peptide, and the inflammatory leucotriene B4 from cutaneous sensory nerves causes local inflammatory responses that trigger psoriasis.<sup>4</sup> Stimulated mast cells secrete a number of proinflammatory cytokines and proteases that act similarly.<sup>4,5</sup>

Carbamazepine significantly inhibits the uptake of noradrenaline (norepinephrine) and blocks a cyclic AMP mediated calcium influx that is associated with neuropeptide release and control of a slow potassium current.<sup>6</sup>

The rapid clearing of erythema, secondary to raised levels of neuropeptides, with carbamazepine may have been mediated through inhibition of these neuropeptides and by inhibition of uptake of noradrenaline. The exacerbation and subsequent resolution of lesions on withdrawal and reinstitution of carbamazepine respectively proves its efficacy in our patient. Also, the clinical remission maintained for 1 year after stopping carbamazepine confirms its therapeutic role in Reiter's syndrome. The therapeutic response seen in our patient conforms to that seen in the HIV-1 positive patient of Smith *et al.*<sup>3</sup>

This apparent success adds carbamazepine to the armamentarium against Reiter's syndrome in an HIV infected patient. This is the first reported case and an evaluation of long term carbamazepine therapy is warranted.

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### Condoms and warts

EDITOR,—Wen *et al.*<sup>1</sup> should be applauded for their attempt to address the key question of whether or not condoms protect people from genital warts. However, some of the major study variables need clarifying, as they did not match up with my knowledge of the Sydney Sexual Health Centre (SSHC) database.

The article discussed the issue of "acquisition of genital warts" and was presented as an incidence study. Cases were defined as: "All

patients with a new diagnosis of macroscopic genital warts who attended SSHC [in] 1996." However, many of these patients had been previously diagnosed with genital warts elsewhere while others had recurrent lesions. In Australia, most genital warts are managed by general practitioners.<sup>2</sup> Consequently, the experience of specialist services is biased towards recurrent and difficult cases. "New diagnosis" in this situation means new to the clinic but not necessarily new to the patient. This means that the main outcome measure was a mixture of incident, prevalent, and recurrent cases, with the possibility that the warts may have affected the behaviour of many of the study subjects.

The SSHC database does document whether a person has previously been diagnosed with HPV infection. To me, the study would have had more validity if patients with a past history had been excluded.

The diagnostic grouping for warts at SSHC does not distinguish between genital and anal lesions. The readers of the journal need to know that many of these male "genital wart" cases would have been homosexually active men with anal warts. This is important as risk factors for penile and anal warts may differ, potentially confusing the results of the present study.

Originally developed as an HIV risk measure, the condom use variable at SSHC only refers to the previous 3 months or since the last registration/disease episode. Wen *et al.*'s article<sup>1</sup> failed to mention that this variable was time limited. As 3 months is the median duration before the appearance of exophytic warts,<sup>3</sup> up to half of the relevant sexual behaviour may have been overlooked.

Finally, the referent group in the table describing condom use deemed as "Not applicable, no sex" should have been more accurately described as "No vaginal or anal sex in the previous 3 months." Many of these people would have practised oral sex or other sexual acts during those 3 months. Others may have ceased practising vaginal or anal intercourse up to 3 months earlier because of their persistent or recurrent warts.

Large relational quality assured clinical databases can be powerful tools for health service evaluation, surveillance, and the generation of research questions. It may be prudent for researchers to engage the people responsible for designing and maintaining those databases to minimise errors of interpretation.

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### Reply

EDITOR,—We are grateful to Dr Dayan for her helpful and constructive comments. The major criticism of our paper relates to the selection of cases, and the possible inclusion

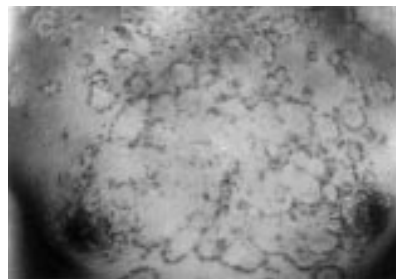


Figure 1 Close view of erythematous annular papules and plaques on chest before carbamazepine therapy.

of prevalent and recurrent cases as well incident cases. However, our concern with this possible bias at the outset of the study led us to exclude all patients with a history of previous genital warts. This included those previously diagnosed at SSHC, and those who gave a history of having their warts managed elsewhere. Consequently, when we state a new diagnosis of genital warts, this is precisely what we mean.

With regard to the conduct of the study, this was performed with the assistance of the current data manager responsible for the SSHC data base, whose help and assistance were duly acknowledged.

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### Photosensitivity reaction to efavirenz

EDITOR,—The non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz is a recent addition to the armamentarium available to physicians in the treatment of HIV infection. However, at present the known side effect profile of this new agent is still in its infancy. We would like to report a case of photosensitivity associated with efavirenz.

A 27 year old white homosexual man was commenced on combivir (zidovudine/lamivudine) and efavirenz in March of 1999. One month later he reported that he was well and had no major side effects associated with his new combination. However, 4 weeks further into treatment he represented with an itchy rash affecting his arms and hands. On examination there was a maculopapular rash over the affected area but there was no oral ulceration, conjunctivitis, or fever. A drug reaction was diagnosed and he was prescribed antihistamines and asked to continue with his medication. One week later the rash had subsided. Then having spent a day outside in the sun he had a florid recurrence of the rash over the exposed areas (arms, back of neck, face, and ears). The rash was significantly worse over his elbows where there was obvious blistering and oedema. His medication was stopped and 3 weeks later the rash had completely resolved. Hepatitis C antibody and porphyria screening were negative. This man had been diagnosed as HIV antibody positive in June 1997. In March 1998 his viral load was 356 790 copies/ml (Roche PCR) and his CD 4 count was  $512 \times 10^6$  cells/l, he was commenced on dual antiretroviral therapy with stavudine and didanosine (patient choice). Initially he did very well as the viral load became undetectable ( $<400$  copies/ml). However, after 9 months on this combination his viral load began to rebound (5192 copies/ml) and a change in antiretroviral therapy was initiated to combivir and nevirapine which he initiated in the normal way (dose escalation at 2 weeks of nevirapine). He was started on this combination as he wished to take a protease sparing regimen. However, 1 week later he developed a rash affecting his entire body, especially his trunk and arms, associated with enlarged lymph nodes and constitutional symptoms, fever, and lethargy. In view of the constitutional symptoms it was decided to stop this present combination. One month later, the

rash had settled, he then commenced combivir and efavirenz.

Photosensitivity in the context of HIV has been reported as a presenting sign of underlying HIV infection in a number of cases.<sup>1-3</sup> In addition to this porphyria cutanea tarda (PCT) has been reported in the context of HIV infection and has been associated with concomitant hepatitis C infection<sup>4</sup>; however, screening for both these conditions was negative. Switching from nevirapine to efavirenz in this context may have been regarded as unwise; however, of 19 patients who have been intolerant of nevirapine secondary to the development of rash, who have switched to efavirenz only nine have developed a mild to moderate rash, of which only two needed to discontinue therapy.<sup>5</sup> Photosensitivity in the context of HIV infection may not only be a presenting condition but also secondary to concomitant treatment.

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### HIV associated cytomegalovirus retinitis in Melbourne, Australia

EDITOR,—We report the results of a 12 year review of human immunodeficiency virus (HIV) associated cytomegalovirus (CMV) retinitis in Melbourne, Australia.

We conducted a retrospective review of all HIV infected patients diagnosed with CMV retinitis at Fairfield Hospital and the Alfred Hospital between 1984 and 1996, aiming to identify factors at diagnosis of CMV retinitis which were predictive of outcome. Both hospitals had the same protocol for the treatment of CMV retinitis and employed 3 monthly ophthalmological screening of all HIV infected patients with CD4 counts of less than  $50 \times 10^6$ /l.

The study outcomes were visual loss and death. Moderate visual loss was defined as a visual acuity of less than 6/12 in the better eye, and severe visual loss as visual acuity of less than 6/60 in the better eye (this is legal blindness in Australia).

CMV retinitis was diagnosed in 212 of 1281 patients (16.5%) with AIDS over the study period. As of June 1998, 193 (93%) had died, at a median time of 36 weeks (range 0-192) from CMV diagnosis. Seventy four patients (35%) developed moderate visual loss at a median time of 23 weeks (range 0-163) and 30 patients (14%) developed severe visual loss at a median time of 35 weeks (range 0-120) from diagnosis of CMV retinitis.

The presence of visual symptoms at diagnosis of CMV retinitis was predictive of the development of moderate visual loss (relative risk 2.1, 95% confidence interval 1.1-4.2). Fifty eight of 138 patients (42%) with visual symptoms at diagnosis developed moderate visual loss, compared with 16 of 64 patients (25%) who were asymptomatic at diagnosis ( $p=0.02$ ). The presence of visual symptoms at diagnosis was not predictive of the development of severe visual loss, or early death ( $p>0.2$ ). Other factors measured at diagnosis of CMV retinitis included the patients' age, CD4 count, weight, visual acuity, and the presence of any previous AIDS defining condition. None of these was associated with the development of visual loss or early death ( $p>0.1$ ).

The advent of highly active antiretroviral therapy (HAART) has resulted in a reduction in the incidence of new diagnoses of opportunistic infections. Prolonged survival times with CMV retinitis have been demonstrated in patients who achieve immunological recovery with HAART.<sup>1,2</sup> The ability to predict those patients who are at highest risk of visual loss may assist in advising those who may reasonably cease maintenance therapy for CMV retinitis following immune restoration. An understanding of the natural history of CMV retinitis in the pre-HAART years remains important in managing patients who are failing HIV therapy.

The only factor measurable at diagnosis of CMV retinitis that was predictive of outcome was the presence of visual symptoms. The use of routine ophthalmological screening in HIV infected individuals with low CD4 counts aims to detect CMV retinitis before visual symptoms occur. It is possible that visual loss may be prevented by detecting disease before retinal damage occurs. A prospective evaluation is needed to confirm this finding.

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